CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40287

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #40-287 SPONSOR : Halsey Drug Company, Inc.
DRUG & DOSAGE FORM : Prednisolone Syrup, USP
STRENGTH (s) : 15 mg/5 mL
TYPE OF STUDY: Waiver
STUDY SITE: N/A.

STUDY SUMMARY : Similar compositions - waiver acceptable

DISSOLUTION: N/A

PRIMARY REVIEWER : Sikta Pradhan BRANCH : I

INITIAL : /S/ DATE : 7/9/98

BRANCH CHIEF : Yih Chain Huang BRANCH : I

INITIAL : /S/ DATE : 7/9/98

DIRECTOR : Dale P. Conner
DIVISION OF BIOEQUIVALENCE

INITIAL : DPC DATE : 7/9/98

DIRECTOR : Douglas L. Sporn
OFFICE OF GENERIC DRUGS

INITIAL : _____ DATE : _____

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA #40-287 APPLICANT: Halsey Drug Company, Inc.

DRUG PRODUCT: Prednisolone Syrup, USP
15 mg/5 mL

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

Prednisolone Syrup, USP
15 mg/5 mL
ANDA #40-287
Reviewer: Sikta Pradhan
XWP #40287W.N97

Halsey Drug Company, Inc.
Brooklyn, New York
Submission Date:
November 24, 1997

Review of a request for Waiver of In-Vivo Bioequivalence Study

The firm has submitted this application to the Agency requesting a waiver of in vivo bioequivalence study requirements for its Prednisolone Syrup, USP 15 mg/5 mL. The firm has stated that, its proposed test product contains the same active ingredient, Prednisolone, as does the listed drug (RLD), Prelone[R] of Muro Pharmaceuticals.

The comparative formulations of the test product and the reference product of Muro are presented below.

Table 1
Comparative Formulations

Ingredient	Test Product (amount/5 mL)	Reference Product (RLD) (amount/5 mL)
Prednisolone Anhydrous, USP	**15 mg**	
Propylene Glycol, USP		
Alcohol 95%, USP		
Benzoic Acid, USP		
Purified Water, USP		
Sodium Saccharin, USP		
Edetate Disodium, USP		
Sugar Fine Granular (sucrose)		
Glycerin, USP		
Caramel Color		
FD&C Red #40 Pure Dye		
Flavor wild cherry PFC-14783		
Artificial Cherry Flavor (WL-1093)		
Dye FDC Blue #1		
Citric Acid, USP		

Comments:

1. Both the test and reference products are labeled for oral administration.

2. The test product contains the same active ingredient, Prednisolone, as does the listed drug (RLD), Prelone^{R} of Muro Pharmaceuticals. The amounts of the inactive ingredients in both the test and reference products are also comparable and are within the acceptable range, except, the amount of the Cherry Flavor WL-1093 which exceeds the maximum concentration of this inactive ingredient previously approved by the Agency in an oral drug product. However, the firm has provided an evidence for the higher exposure/day of the Cherry Flavor WL-1093 in an approved application (N88-739) than in the proposed test product (see Exhibits 1&2, attached). Therefore, the higher amount of the Cherry Flavor WL-1093 mg/5 mL) does not affect the safety of the proposed drug product.

3. Hence, the test product is quantitatively and qualitatively similar to the innovator product, Prelone^{R} of Muro Pharmaceuticals, and therefore, the request for waiver of <u>in-vivo</u> bioequivalence study is acceptable.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Halsey Drug Company, Inc. demonstrates that the test product, Prednisolone Syrup, USP 15 mg/5 mL falls under 21 CFR Section 320.22(b)(3) of the Bioavailability/Biequivalence Regulations. The waiver of <u>in vivo</u> bioequivalence study for the

proposed test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test solution formulation to be bioequivalent to Prelone^{R} manufactured by Muro Pharmaceuticals.

/S/

Sikta Pradhan, Ph. D.
Division of Bioequivalence
Review Branch I

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FT INITIALED YCHUANG

/S/ 7/9/98

Concur: /S/ Date: 7/9/98

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

cc: AND # 40-287 (original, duplicate), HAD-652 (Huang, Pradhan), HAD-650 (Director),Drug File, Division File.